Host-Pathogen Interaction (Immunology)
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Module No # 09
Lecture No # 49
Introduction to the Adaptive Immunity

So in previous session we have learnt about the compleiments and we have studied various complement pathway that is classical pathway we have studied alternative pathway and lectin pathway. So let us move on and with complement I almost completely finished the innate immunity now let us move to the adaptive immunity. So in adaptive immunity we will study I will introduce you with antigen, what is antigen and immunogen? And we will also discuss about the B cell how the B cell produce antibody.

What kinds of antibodies are produced and I am not going to take great detail about the antibody diversity. But I will definitely touch upon how the diversity is achieved in case of B cells which produce different kinds of antibody. And I will also touch upon the T cell, diversity the T cell for every antigen or for every antigenic determinant there is a specific T cells.

So I will touch upon the diversity component in both b and t cells I will just explain you the key concepts although I am not going to take you in more finer molecular detail because that is not in is in the scope of this course. And then thereafter we will move on various host pathogen interaction will take up viruses and then we will take up bacteria so and so. So let us begin with adaptive immunity so here you know that adaptive immune response is basically depend on the innate immune response.

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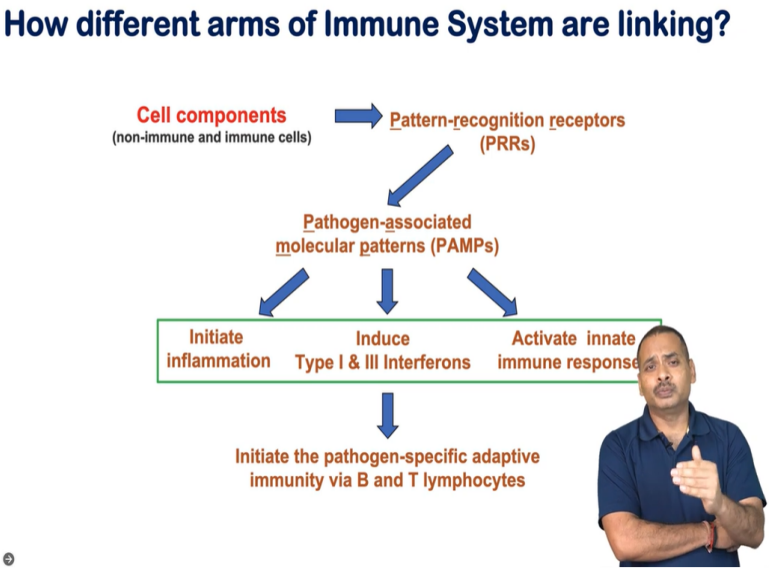

So you are probably familiar with this slide probably I have shown you in previous session but I will repeat you. And here I will emphasize how the, adaptive immune response is elicitated? You know the cellular component of innate immunity is basically consists of almost all cells of the host which is non-immune cell. And there are professional immune cells like macrophages dendritic cells and Eosinophil, Neutrophil, Basophils, natural killer cells and all those things.

Most of these cells express the patternt recognition receptor, you know now you can understand very well about the pattern recognition receptor there are several families of pattern recognitions receptor. And the overall outcome of activation of this PRR mediated signaling is induction of inflammatory cytokines. So these pattern recognition receptor basically since the signature molecule of microbial pathogen which we you know that we call it as a pumpsPAMPs.

And upon sensing these pamps basically it initiated inflammation I have discussed several sessions about the inflammation now you are very well clear about the inflammation. And then it also activate the innate immune response means that the microbial pathogen will be basically more actively phagocytosed by the these innate immune cells. So that I mean to say that activate innate immune response.

So more readilyRidily phagocytose more readily production of hydrolyasesis in the endo lysosome or phagosomes and there will be a more aggressive production of reactive oxygen and nitrogen species that I mean about this activate innate immune responses. And it if it is the

virus infection it will induce the type 1 and type 3 interferon which basically clear the viruses by various mechanism.

I have, explained you in previous session how these viruses are cleared by shutting down the metabolic machinery and so on so forth. So far everything is good but if the pathogen is not cleared then what will happen so if the innate immune system is not able to clear these kind of infection then that will trigger the development of more specific immune response. And more specific immune response means, there will be a activation of some key lymphocytes.

As you can see here there are 2 key lymphocytes that is B cells and T cells. So these B and T cells will generate a highly specific molecule which will be basically help in clearing or elimination of this microbial pathogen. And these in case of B cell these B cells will produce a specific antibody of highly specific, antibody against the microbial pathogen. There will be a repertoire of antibodies so not only one antibody there will be a array of antibody which is generated against this microbial pathogen.

And once this antibody is generated so every antibody there; are several kinds of antibody which I will discuss in subsequent session the different kinds of antibody. All these antibody has some specific, downstream function so once this antibody is generated then this microbial pathogen will be eliminated. On another hand this will be also trigger the development of antigen specific T cells.

So antigen is specific T cells they have also variety of function in if you look at the t cells there are 2 major kinds of T cell. One is Tth cells which I have also discussed in previous session but I am, bringing all those key points which is associated with adaptive immunity. So the T cells are T helper cells and cytotoxic T cells and this T helper cells can differentiate into particular T helper cells for example th 1, th 2, th 17 so and so forth.

And these particular kinds of th cells will develop a particular kind of immune responses a very simple if the th1 response will be elicitated, then there will be a killing of intracellular pathogen the killing of intracellular bacteria. And if there will be a th2 response against that microbial pathogen then that will trigger more prominent B cell mediated immune response antibody production it may trigger the allergy and so on so forth.

So this is the more pathogen specific immune response and these highly pathogen specific, immune response we call it as an adaptive immunity. So in adaptive immunity basically we

talk about the B cells and T cells and how the b cells are developed as you know that B cells are basically produced in bone marrow and they will educate and then there will be a generation of naive B cells. And then these B cells will educate and then in a lymph node and then, it will become a antigenous specific immunocompetent B cells.

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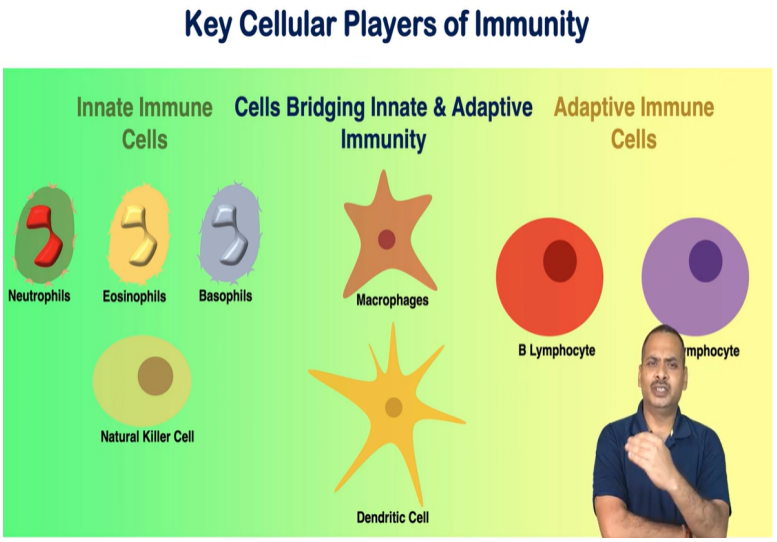

So let us move on here I will also talk about the key players of the immunity which I have already discussed in when I have taken the cell component of immunity. As you know that these; are the innate immune cell like Neutrophil, Eosinophil, Basophils and Natural killer cells. So they are the key innate, immune cells and adaptive immune cells are B lymphocyte and T lymphocyte.

And here you can see that these cells the macrophages and the dendritic cells they are kind of bridge between innate and adaptive immunity I will tell you how? You know that macrophages and dendritic cells they can phagocytose the microbial pathogen. And upon phagocytosis they can produce the inflammatory, cytokines. So these inflammatory cytokines can recruit other immune cell at the site of infection.

On another hand these macrophages can eat up those microbial pathogen and then they can present it to the present the antigen of these microbe over the cell membrane along with one family of molecule which we call it as a MHC and macrophages can present the antigen along with MHC class 2 molecule. And this MHC class 2 molecule along with antigen is needed for the development of t cell mediated immune response.

So you can understand these cells are linker between both innate and adaptive immune response. Similarly the Dendritic cells so Dendritic cells can also induce innate immune responses in terms of production of innate cytokines and they can also process the microbial antigen and they can present along with MHC class 2 molecule. And they can also induce the differentiation of th cells and depends on type of subtype of th cells the immune response will be developed.

In addition, you know that all nucleated cells can express MHC class one molecule all nucleated cells so here there is one exception do not forget that is RBC do not present, any antigen. So these all rest of non-immune cells they express MHC class one molecule and they play a very important role during virus infection. So these MHC class 1 molecule can activate cytotoxic T cells and once the cytotoxic t cells will be developed then these cells will basically clear the viral infection or trigger the apoptosis of target cell or death of house cells.

So, in that way here you can see that all cells whether it is an immune cell or non-immune cell they are basically a linking between innate as well as adaptive immunity. The non-immune cell how they are linked how they are involved in innate immunity. You can understand that once this non-immune cells they are infected with say virus then this can most of these cells can produce type 1, interferon and to some extent inflammatory cytokine.

So in that way they are playing important role in innate immunity on another hand these cells can also present the antigen along with MHC class 1 molecule and then they can activate CD 8 T cells or cytotoxic T cells. So in that way they are also involved in adaptive immunity so here you can see there is a junction and this is a junctional, point between innate and adaptive immunity. Now this is a good time that I should discuss the or I should compare both innate and adaptive immunity.

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Comparison of innate and adaptive immunity

S.N.	Characteristics	Innate Immunity	Adaptive immunity
1	Presence	Innate immunity is already present in the body.	Adaptive immunity is developed upon exposure to a foreign substance.
2	Specificity	broad-Specificity	Highly Specific
3	Response	Fights with any living and non-living foreign entities	Develop highly specific immune response, if not cleared by innate immunity
4	Response time	Rapid (minutes to hours)	Slow (in days or 1-2 weeks)
5	Potency	Limited and Lower potency	High potency
6	Time span	Every time the response is generated irrespective to the no. of exposer.	Once immune response developed. The immunity can be lifelong or short depends on pathogen.

So here you can see that there are some characteristic which is given in the second column and what kind of innate immunity is there and what kind of adaptive immunity is there? So the first is presence the innate immunity is already, present in the body it is not it is always there you can understand anatomical barrier chemical barrier. So any anything will come there will be a production of these chemical mucus hydrochloric acid enzymes reactive oxygen species reactive nitrogen species it is always there.

And in case of adaptive immunity it is developed upon exposure to the foreign substance what I mean to say that once the pathogen or microbe is entered in the host then there will be a development of adaptive immune response if it is not cleared by the innate immunity. Specificity if you see the previously people thought that innate immune immunity has no specificity. But and after learning about the pattern recognition receptor I can say or you can understand that innate immunity do, have a broad specificity.

They can sense the family of molecule and induce appropriate innate immune response. On another hand adaptive immunity is highly specific I will convince you by this statement in subsequent session. But for time being you can understand that the antibodies which is produced against particular antigen is highly specific. So that is why adaptive immunity has a high, specificity the t cells which is recognizing the antigen along with MHC molecule they are also highly specific it is not they do not have a broad specificity.

So you can understand that adaptive unity has a very high specific specificity response if you look at the response in case of innate immunity can fight with any living and non-living foreign entities. It is a irrespective of whether it, is a living or it is non-living if the host is

exposed to some dust so that can also elicitate the appropriate innate immune response. For example more production of mucus so and so forth adaptive immune developer highly specific immune response if not cleared by the innate immunity.

I have explained you in previous slide that if the innate immune system does not clear the microbial, pathogen then this will trigger the development of an adaptive~~ctive~~ immune response. Response time in case of innate immunity the response time is rapid it is within a minute or maximum to few hours. But adaptive immunity development of adaptive immune response takes more time it depends on what kind of microbial pathogen is there. and whether this microbial infection is first time or second time.

So if the host is exposed first time with a particular microbial pathogen then it will take a longer time to develop the adaptive immune response. If the same pathogen is infecting the host second time then it will take relatively less time. So but in both case it will take a reasonably good amount of time it may take a day a few days to couple of weeks' time. Potency if you see that, innate immune response all those innate immune responses are having a limited potency.

For example blood clotting blood clotting is also innate immune response inducing fever is also innate immune response they have a limited effect and they have a limited potency. On another hand adaptive immunity which is highly specific to the pathogen they are highly potent. Basically once that adaptive~~active~~, immune response is appropriate adaptive immune response is developed then the microbial infection can be eliminated or decline.

Start declining time span so every time the response is generated irrespective of number of exposure. For example an individual is exposed with say some ~~strip~~ staphylococcus aureus so the innate immune response against staphylococcus the first time, will be will be same as the second time there will be a no change. But if it is inducing the adaptive immune response the response time will depend on the type or times of exposure.

If it is the first time then it will take longer time and if it is a second time then it will take a shorter time. And it also depends on that particular microbial pathogen for in case of adaptive, immunity sometimes this will have a very long remembrance. Or this the immune response which is which is developed first time will remain stay in the host for longer time or sometime it will be a shorter time depends on the microbial pathogen.

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Comparison of innate and adaptive immunity

S.N.	Characteristics	Innate Immunity	Adaptive immunity
7	Inheritance	Innate type of immunity is generally inherited from parents and passed to offspring.	Adaptive immunity is not passed from the parents to offspring, hence it cannot be inherited.
8	Intensity of immune response	Cannot react with equal potency upon repeated exposure to the same pathogen.	Adaptive system can remember the specific pathogens which have encountered before.
9	Presence	Present at birth	Develops during a person's lifetime and can be short-lived.
10	Allergic Reaction	None	Immediate and Delay hypersensitivity
11	Memory	No memory	Long term memory

Another is inheritance so innate type of immunity is generally inherited from parent and passt to the office spring. So basically this is a, jam line encoded genes are there over there is a there will be a no change. But in case of adaptive immunity there is a presence of a gene segment which will make a specific type of B cells against particular antigen. So that may change but the basic framework is also inherited but the immune response the development of immune response may vary to some extent.

That what I want to say, that the inheritance in both case there is an inheritance but the in case of innate immunity the germline encoded receptor they do not change they just whatever germline encoded genes are there they will express and induce the immune response. But in case of adaptive immunity there will there is a gene segments which will rearrange and then that will develop a particular B cell or T cell, response so that may change this is not inherited.

Another point is in intensity of immune response so innatelet immunity cannot react with equal potency upon repeated exposure to the same pathogen I have explained you. In case of adaptive immunity the adaptive immune system can remember the specific pathogen which have encountered before. Again the innatedinette immunity is present, since birth and adaptive immunity is basically developed during the person's lifetime and can be short-lived it can be short-lived it can be a long lived.

So here I am just trying to explain this point so for example there are mirror image twins they having they are having a same genetic makeup and one individual who lived in very clean environment and they are not that, individual is not exposed to the lot of antigen. On another

hand another individual that individual is living in a not so clean environment and they that individual is keep on exposing with various microbial pathogen.

So this individual will have a really different set of immunity it is not although the genetic is same but this the individual who lived in not so clean environment, their immunity is much more educated much more trained there is a term known as trained immunity trained innate immunity also is there. So that immunity will protect that individual from much more wider range of microbial pathogen so that what I want to say that.

Allergic reaction in case of in innate immunity there is no such kind of term is there so we do not say that, this is an innate immune response the allergic reaction. But in case of adaptive immunity~~unity~~ it is a basically associated with the allergy is associated with various kind of adaptive immune response antibody mediated or T cell mediated it depends. There is variety of allergic reaction and all these allergic reactions are basically dependent on adaptive immune response.

Memory innate immunity they do, not have a memory but these days there is a some term known as trained immunity or so those school of thoughts say that they do have some kind of memory but it is not very clear. In textbook it is very well documented that the innate immunity they do not have a memory. But on another hand adaptive immunity has a very long memory or long term memory that depends on, the microbial pathogen and this memory is very important for making vaccine or developing immunity against the microbial pathogen.

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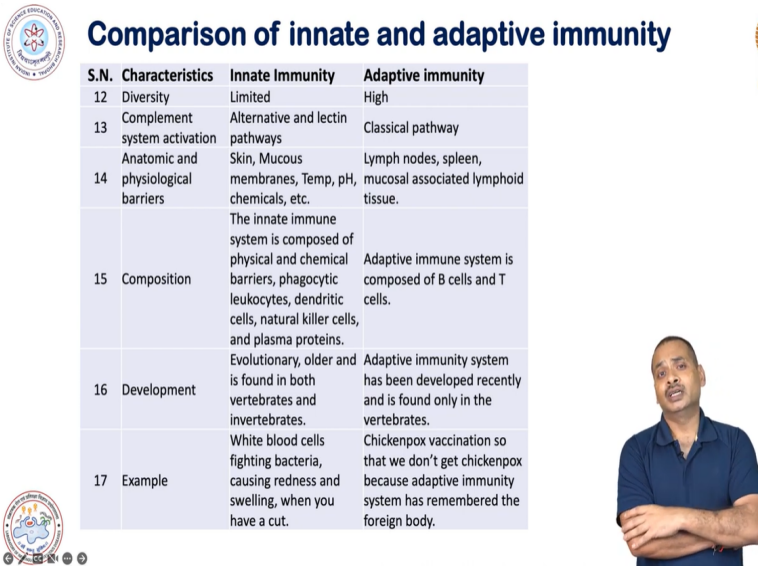

Another is diversity so innate immunity has a limited diversity but on another hand adaptive immunity has a huge diversity. There is a endless number of antibody can be produced by the host or there can be endless number of antigen specific T cells can be generated. So the adaptive immunity has a huge diversity third is complement so alternative pathway and lectin pathway is more like innateer immunity although they have a some level of specificity for the mannose residue in case of lectin pathway.

On another hand the classical pathway is purely or it is it has a both; component of innate and adaptive immunity the innate component is this develops production of, these complement protein and the adaptive component is the activation basically takes place through the antibodies. So that is that is the classical pathway anatomic and physiological barrier in case of innate immunity you know very well there is skin mucous membrane.

There will be increase in temperature that is fever which will inhibit the growth of microbial pathogen the PpH and various, chemicals such as hydrochloric acid present in our stomach. And there are some substances produce over the skin that is certain sebaceous secretion that will change the PpH drastic change the PpH so that the pathogenic microbial pathogen cannot grow.

On another hand the adaptive immune organs are lymph node spleen or mucous associated lymphoid tissues. Composition of the innate immune system is basically composed of a physical chemical microbiological you remember we have discussed about the microbiological barrier. And there is a phagocytic cells the dendritic cells natural killer cells and there are various soluble protein. If you remember there are CRP C reactive protein mannose binding lectin MBL so all these, are the basically component of innate immunity.

On another hand the adaptive immunity is basically composed of B lymphocyte and T lymphocyte development. So innate immunity is a evolutionary it is a very old and it is found in both vertebrate and invertebrates. The adaptive immunity is relatively more new or recent I have explained you when I have initiated innatelet immunity.

So, adaptive immune system has been developed recently and found only in the vertebrates example there are various example white blood cells fight with bacteria that cause bacterioalysis inducing various signatures of inflammation and that is redness swelling pain and there is a increase in temperature. In case of adaptive immunity the chickenpox

vaccination so that we do not get chickenpox. So the host is exposed with the chickenpox antigen so that the host will not develop again chickenpox.

Because of development of appropriate adaptive immunity that is B cell and T cell mediated immunity and that will be remembered by the host. And then they will keep the battery of those antibody producing cells that is B cells and T cells and in that way the host is protected. So this is all about the discussion about the innate and adaptive unity this is a very good comparison.

Now I have a one short video which will basically show you the whole immunity the innate and adaptive immunity and then you this will be a very helpful in understanding overall this innate and adaptive immunity and the junction between innate and adaptive immunity you can, watch and enjoy.

(Video Starts: 30:05)

Every second of your life you are under attack billions of bacteria viruses and fungi are trying to make you their home. So our bodies have developed a super complex little army with guards soldiers intelligence weapons factories and communicators to protect you from well dying. For this video let us assume the immune system has 12 different jobs for example kill enemies communicate, etc. And it has 21 different cells and protein forces these cells have up to 4 different jobs let us assigned them here are the interactions.

Now let us make this understandable first of all let us add colors to the jobs now let us illustrate the cells the central color represents the main job of the cell while the surrounding ones represent secondary duties. Now the immune system looks, like this now the interactions is not this complexity just awesome for this video we will only talk about these cells and ignore the rest.

So what happens in the case of an infection? It is a beautiful day when suddenly a wild rusty nail appears and you cut yourself the first barrier of the immune system is breached your skin nearby bacteria seesason the opportunity and enter your wound they start, using up the body's resources and double their numbers about every 20 minutes. At first they fly under the radar but when a certain bacterial population is reached they change their behavior and start to damage the body by changing the environment around them.

The immune system has to stop them as fast as possible first of all your guard cells known as macrophages intervene they are huge cells that, guard every border region of the body. Most of the time they; alone can suffocate an attack because they can devour up to 100 intruders each. They swallow the intruder hole and trap it inside a membrane then the enemy gets broken down by enzymes and is killed.

On top of that they cause inflammation by ordering the blood vessels to release water into the battlefield so fighting becomes easier. You, notice this as a very mild swelling when the mactrophages fight for too long they call in heavy backup by releasing messenger proteins that communicate location and urgency. Neutrophiles leave their patrol roots in the blood and move to the battlefield.

The neutrophiles fight so furiously that they kill healthy cells in the process on top of that they generate barriers that trap and kill the bacteria. They are indeed so deadly that they evolved to commit suicide after five days to prevent them from causing too much damage. If this is not enough to stop the invasion the brain of the immune system kicks in. The dendritic cell gets active it reacts to the signals of the soldiers and starts collecting samples from the enemies.

They rip them into pieces and present the parts on their outer layer now, the dendritic cell makes a crucial decision should they call for antivirus forces that eradicate infected body cells or an army of bacteria killers. In this case antibacterial forces are necessary it then travels to the closest lymph node in about a day. Here billions of helper and killer t cells are waiting to be activated. When T cells are born they go through a difficult and complicated training, process and only a quarter of survives.

The surviving cells are equipped with a specific setup and the dendritic cell is on its way looking for a helper T cell with a setup that is just right it is looking for a helper t cell that combined to the parts of the intruders which the dendritic cell has presented on its membrane. When it finally finds one the chain reaction takes place the helper T cell is activated it quickly duplicates thousands of times.

Some become memory to cells that stay in the lymph node and will make you practically immune against this enemy. Some travel to the field of battle to help out and the third group goes on to travel to the center of the lymph node to activate a very powerful weapons factory.

Like the T cells they are born with a specific setup and when a B cell and a T cell with the same setup meat hell breaks loose.

The B cell duplicates rapidly and starts producing millions of little weapons they work so hard that they would literally die from exhaustion very fast. Here helper T cells plays another important role they stimulate the hard-working factories and tell them do not die yet we still need you keep going. This also ensures that the factories, die of the infection is over so the body does not waste energy or hurt itself.

But what is produced by the b cells you have heard of them of course antibodies little proteins that are engineered to bind to the surface of the specific intruder. There are even different kinds of antibodies that have slightly different jobs the helper T cells tell the plasma cells which type is needed the most in this, particular invasion. Millions of them flood the blood and saturate the body meanwhile at the site of infection the situation is getting dire.

The intruders have multiplied a number and start hurting the body guard and attack cells fight hard but also die in the process helper T cell support them by ordering them to be more aggressive and to stay alive longer. But without help they cannot overwhelm, the bacteria but now the second line of defense arrives. Billions of antibodies flood the battlefield and disable lots of the intruders rendering them helpless or killing them in the process.

They also stun the bacteria and make them an easy target their back is built to connect to carousels so they can connect and kill the enemy more easily. Macrophages are especially good at numbing up the bacteria, which antibodies have attached to. Now the balance shifts in a team effort the infection is wiped out at this point millions of body cells have already died no big deal the losses are quickly replenished.

Most immune cells are now useless and without the constant signals they commit suicide so as not to waste any resources but some stay behind the memory cells. If this enemy is encountered ever again, in the future they will be ready for it and probably kill it before you even notice. This was a very simplified explanation of parts of the immune system at work can you imagine how complex this system is even at this level when we ignore so many players and all the chemistry life is awfully complicated.

But if we take the time to understand it we always encounter endless wonders and great beauty.

(Video Ends: 36:37)

So I hope this is a very interesting video it is a very short and very simple and explaining almost all immunity. You can see that there are involvement of innate immunity, adaptive immunity and how the T helper cell is stimulating the antigen presenting cells and B cells in order to keep the fight against microbial pathogen. So with this I will stop this session and in next session I will start with, antigens. We will discuss about the antigen and in subsequent session I will discuss about the properties of antigen thank you very much.